

REMARKS

Claims 9, 16, 19, 20 and 21 are pending in this application. Claims 14, 17, 18, 22 and 24 are canceled without prejudice or disclaimer. Claims 9 and 16 are amended for clarity. Claims 9 is amended for clarity, without prejudice or disclaimer, to recite that "the soluble derivative consists of: a fragment of complement receptor 1 (CR1), wherein the CR1 fragment consists of first three Short Consensus Repeats (SCR1-3), and has a complement inhibitory activity, wherein the fragment is conjugated to myristoyl and a basic amino acid sequence, according to SEQ ID NO: 1; and ...the physiologically acceptable flush storage solution is SOLTRAN, which is a kidney perfusion solution...." Claim 16 is amended, also for clarity, to recite that "the fragment of complement receptor 1 (CR1) consists of first three Short Consensus Repeats (SCR1-3) and has the sequence according to positions 2 to 197 of SEQ ID NO.1." The amendments are supported by the specification (see specification, for example, page 4, lines 28-31, page 13, lines 15-20, pages 19-21, Examples 1 and 2). Therefore, no new matter is introduced. The Office Action is discussed below:

Objection to the Specification:

On page 2 of the Office Action, the examiner has objected to the specification and alleged that some paragraphs on pages 12 and 13 of the specification are crossed out. Applicants could not find any crossed-out paragraphs on pages 12 and 13 of the specification as filed. However, applicants refer the examiner to the amendments (to the specification, pages 12-13), as filed on December 7, 2001, in which page 12, line 44 through page 13, line 12 are amended to insert sequence ID Nos. Applicants are willing to submit replacement sheets, if necessary, and request the examiner to provide copies of the alleged crossed-out paragraphs.

Claim Rejection under 35 USC § 112, second paragraph:

On pages 2-3 of the Office Action, the examiner has rejected claims 9, 14, 16-22, and 24 allegedly as being indefinite. According to the examiner, claim 9 is unclear

as to whether there is an order prescribed in subsection (2) of the claim. Applicants indicate that amendment, without prejudice or disclaimer, to claim 9 subsection (2) moots the rejection.

Regarding claim 24, the examiner asserts that the parentheses are unclear, whether the kidney perfusion solution can be SOLTRAN, or is SOLTRAN merely an example of the solution to be used. Applicants cancel claim 24 without prejudice or disclaimer, however, the subject matter of the cancelled claim is added on to claim 9 to recite that "SOLTRAN, which is a kidney perfusion solution".

In view of the above, withdrawal of the indefiniteness rejection is solicited.

Claim Rejection under 35 USC § 112, first paragraph:

Written Description Rejection:

On pages 3-6 of the Office Action, the examiner has rejected claims 9, 14, 16-22 and 24 allegedly for failing to comply with the written description requirement.

The examiner asserts that claim 9 recites a fragment comprising "any sequence" of SEQ ID NO:1 having complement inhibitor activity and opined that the fragment is reading on virtually no structure, and only is reading on the activity of the fragment. Therefore, according to the examiner, the written description requirement is not satisfied because the structure of the fragment does not correspond with its function. Applicants respectfully disagree with the examiner and indicate that the examiner has misread the claim as the term "any sequence" is not recited in the claim. However, for additional clarity, applicants amend the claim to recite that "the soluble derivative consists of: a fragment of complement receptor 1 (CR1), wherein the CR1 fragment consists of first three Short Consensus Repeats (SCR1-3), and has a complement inhibitory activity, wherein the fragment is conjugated to myristoyl and a basic amino acid sequence, according to SEQ ID NO: 1...." Therefore, the written description requirement is satisfied.

Applicants indicate that the examiner also has misread claim 16, because, the claim does not recite "any sequence" of SEQ ID NO:1. However, for additional clarity, applicants amend the claim to recite that "the fragment of complement receptor 1 (CR1) consists of first three Short Consensus Repeats (SCR1-3) and has the sequence according to positions 2 to 197 of SEQ ID NO.1." Therefore, applicants submit that the written description requirement is satisfied for claim 16 as well.

Applicants also indicate that amendments to claim 9 and cancellation of claims 14, 17, 18 and 22, without prejudice or disclaimer, moot the examiner's concerns regarding claim 9 subsections (2)(a) and (2)(b) and related claims. Therefore, withdrawal of the written description requirement is solicited.

Enablement Rejection:

On pages 6-8 of the Office Action, the examiner also has rejected claims 9, 14, 16, 18-22 and 24 under 35 U.S.C. 112, first paragraph, allegedly because the specification, while being enabling for peptidic membrane binding element comprising SEQ ID NOs:7-11, does not reasonably provide enablement for all other undisclosed peptide membrane-binding elements that have basic amino acids and non-peptidic membrane binding elements with acyl groups. Applicants disagree with the examiner, however, in order to expedite the prosecution, applicants cancel claims 14, 18, and 22-24; amend claim 9 to recite that "the soluble derivative consists of: a fragment of complement receptor 1 (CR1), wherein the CR1 fragment consists of first three Short Consensus Repeats (SCR1-3), and has a complement inhibitory activity, wherein the fragment is conjugated to myristoyl and a basic amino acid sequence, according to SEQ ID NO: 1; and ...the physiologically acceptable flush storage solution is SOLTRAN, which is a kidney perfusion solution..." and amend claim 16 to recite that "the fragment of complement receptor 1 (CR1) consists of first three Short Consensus Repeats (SCR1-3) and has the sequence according to positions 2 to 197 of SEQ ID NO.1."

In view of the all above, applicants submit that the claimed methods are supported by enabling disclosure, accordingly, request withdrawal of the enablement rejection.

Claim Rejection under 35 USC § 102(e):

On pages 8-9 of the Office Action, the examiner has maintained the rejection of claims 9, 14, 16, 17, and 19-22 allegedly as being anticipated by Rittershaus *et al.* (U.S. 6,193,979). On page 9 of the Office Action, the examiner also maintained the rejection of claims 9, 17, and 18 under 35 U.S.C. 102(e) allegedly as being anticipated by Smith *et al.* (U.S. 6,713,606 B1).

The examiner believes that acyl groups are present where carbohydrate side chains of complement glycoproteins may be selectively oxidized to generate aldehydes and aldehydes have acyl groups in their structure. Therefore, the examiner still believes that the anticipation rejection is proper. Applicants respectfully disagree with the examiner and traverse the rejection. Simply put, Rittershaus does not teach or suggest the particular selected combination of soluble polypeptide and non-reducing flush-storage solution as claimed in this application.

Applicants reiterate that "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). See MPEP § 2131.01 (Rev. 6., September 2007). Applicants review below the references with these concepts in mind.

Applicants also wish to remind the examiner that Rittershaus *et al.* disclosed a CR1 protein which was not the CR1 fragment recited in the claims (see amended claim 9, for example), but was modified by glycoform manipulation. Such modification is not possible for SEQ ID NO:1, which differs from Rittershaus' protein because, among other things, SEQ ID NO:1 lacks a single N-linked glycosylation site from which a sialyl Le^x structure could be attached. Thus, even if the composition of Rittershaus *et al.*

were to be retained in ischemic organs, which the examiner has not demonstrated, such a molecule could not be derived from the region of CR1 utilized in the instant invention. In sum, because Rittershaus does not disclose the same type of molecule as claimed, thus cannot anticipate the claimed invention.

Turning to Smith, applicants maintain that Smith discloses the use of compositions including CR1 fragments (such as the construct APT 070) for treatment of injury which has occurred by ischemic conditions. In contrast, the present invention is intended to pre-treat "healthy" organs before transplant/storage so as to prevent ischemic injury. Therefore, Smith disclosure does not anticipate the claimed invention.

Applicants reiterate that Smith discloses soluble derivatives of soluble peptides that can be used according to the invention. The present claims, however, are not solely directed to such composition or derivatives, but rather inventive selection of the use of one specific derivative. Such claims are specifically permitted under 35 USC §§ 100(b), 101. In this regard, applicants refer to the following quotations of 35 U.S.C.:

35 U.S.C. 100 Definitions.

When used in this title unless the context otherwise indicates -

- (b) The term "process" means process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material. (emphasis added).

35 U.S.C. 101 Inventions patentable.

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title. (emphasis added).

The claimed methods require the presence of the soluble derivative in an isolated organ. Accordingly, the invention claimed here requires the organ to be in an *ex vivo* environment, which precedes transplantation.

In order to further distinguish the claimed invention from the cited references and for additional clarity, applicants amend claim 9 by incorporating the subject matter of canceled claim 24 (that "the physiologically acceptable flush storage solution is

SOLTRAN, which is a kidney perfusion solution"), which was not subject to anticipation rejection. Accordingly, the cited references do not disclose each and every elements of the claimed invention.

In view of the above clarifications, arguments and amendments, applicants respectfully request withdrawal of the anticipation rejection.

Claim Rejection under 35 USC § 103(a):

On pages 9-11 of the Office Action, the examiner also has maintained the rejection of claims 9, 14, 16-21 and newly rejected claim 24 under 35 U.S.C. 103(a) allegedly as being unpatentable over by Rittershaus *et al.* (U.S. 6,193,979 B1) in view of Smith *et al.* (U.S. 6,713,606 B1).

The examiner states that the rejection over Smith is correct because Smith *et al.* teach that: 1) CR1 and membrane binding elements are consistent with claim 17; 2) soluble CR1 polypeptide is derivatized with a myristoyl group consistent with claim 18; and 3) the claimed peptides are used for Post-Ischemic Reperfusion Conditions. Applicants disagree with the examiner and refer to above clarification regarding alleged anticipation rejection that Smith does not disclose the claimed invention.

Applicants point out that the examiner did not provide factually-supported rationale for performing a method that would require substituting Rittershaus *et al.* transplant compound with Smith *et al.* compound. However, the examiner believes that a person skilled in the art would have been motivated to make the above substitution, because both compositions are taught as having uses in the prevention of post-ischemic reperfusion injuries, and one would expect a success in perfusing an organ with the myristoylated CR1 polypeptide of Smith *et al.* Again, applicants disagree with the examiner, and refer to the dictates of MPEP that:

"FACT THAT REFERENCES CAN BE COMBINED OR MODIFIED
**MAY NOT BE SUFFICIENT TO ESTABLISH PRIMA FACIE
OBVIOUSNESS

The mere fact that references can be combined or modified does not render the resultant combination obvious unless **the results would have been predictable to one of ordinary skill in the art. *KSR International Co. v. Teleflex Inc.*, 550 U.S. ___, ___, 82 USPQ2d 1385, 1396 (2007)...”

“MERE STATEMENT THAT THE CLAIMED INVENTION IS WITHIN THE CAPABILITIES OF ONE OF ORDINARY SKILL IN THE ART IS NOT SUFFICIENT BY ITSELF TO ESTABLISH PRIMA FACIE OBVIOUSNESS

A statement that modifications of the prior art to meet the claimed invention would have been "well within the ordinary skill of the art at the time the claimed invention was made" because the references relied upon teach that all aspects of the claimed invention were individually known in the art is not sufficient to establish a *prima facie* case of obviousness without some objective reason to combine the teachings of the references. *Ex parte Levengood*, 28 USPQ2d 1300 (Bd. Pat. App. & Inter. 1993). ***[R]ejections on obviousness cannot be sustained by mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *KSR*, 550 U.S. at ___, 82 USPQ2d at 1396 quoting *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006)."

See MPEP §2143.01 (III-IV) at 2100-140 (Rev. 6., September 2007).

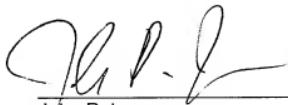
In this case, applicants point out that the examiner has not provided any factual rationale to support the purported combinations. Applicants, therefore, submit that a *prima facie* case of obviousness has not been established by the examiner. Accordingly, withdrawal of the obviousness rejection is solicited.

REQUEST

Applicants submit that the claims 9, 16, 19, 20 and 21 are in condition for allowance, and respectfully request favorable consideration to that effect. The examiner is invited to contact the undersigned at (202) 416-6800 should there be any questions.

Respectfully submitted,

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Date



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